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# RESERVOIR-TYPE VAGINAL RINGS FOR CONTROLLED RELEASE OF ISOSORBIDE MONONITRATE

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**Background:** Induction of labour, i.e. starting labour artificially, is often needed in the presence of unfavorable cervix. Prostaglandins are the most commonly used agents in cervical ripening and inducing labour, which also cause uterine contraction and require close monitoring of patients in hospital. Isosorbide mononitrate (ISMN) has gained considerable attention in the application of cervical ripening. Unlike prostaglandins, the use of ISMN allows cervical ripening to occur without uterine contractions, thus might be suitable to be performed in an outpatient environment. This study focuses on evaluating the potential for controlled release of ISMN from silicon elastomer vaginal rings over 14 days, with the aim to develop a ring device for cervical ripening and induction of labour in an outpatient setting.

**Methods:** Reservoir-type silicone elastomer vaginal rings comprising an ISMN-loaded core and a mon-medicated sheath were manufactured using injection-molding technologies. Rings with different core-lengths, excipients in the sheath (5%, 10% and 20% sucrose) or orifices in the sheath were prepared. DSC testing and *in vitro* release testing were performed on the ring devices.

**Results:** For the rings without sucrose and the rings with orifices in the sheath, a relatively large amount of ISMN was released on Day 1 (7.2 and 10.3 mg, respectively), i.e. 'burst effect', and slower release was observed in the following days with Day 11 release 4.4 and 5.1 mg, respectively. In the contrast, no burst effect was observed for rings containing sucrose in the sheath. The daily release of ISMN for rings containing 5%, 10% and 20% sucrose kept increasing from Day 1 (4.6, 4.2 and 3.9, respectively), which reached the maximum on Day 8 (5.2, 6.0 and 7.9, respectively), and started decreasing thereafter. All cumulative ISMN release versus time profiles were linear, indicating a permeation-controlled release mechanism. The addition of up to 10% sucrose didn't significantly affect the release rate of ISMN. There is no significant difference in the ISMN release rate for rings without sucrose and the rings with 5% and 10% sucrose. Compared with three types of rings, the ring containing 20% sucrose and the ring with windows in the sheath had faster release rates, which were 6.37 and 6.29 mg/day.

**Conclusions:** Vaginal rings which can deliver ISMN at a constant rate were successfully developed in this study. The release rate of ISMN from the ring devices can be adjusted by the core-length, sheath compositions (the addition of excipients) and novel ring designs (orifices in the sheath). These vaginal ring devices which could enable controlled administration of small amount of ISMN vaginally might be potentially useful for cervical ripening in an outpatient environment, offering greater maternal satisfaction and lower costs.